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Supplemental material

Clinical translation of noninvasive intracranial pressure sensing with diffuse correlation spectroscopy

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Supplemental Materials and Methods

Section 1. Signal acquisition

Details on the theory and instrumentation of Diffuse Correlation Spectroscopy (DCS) can be found elsewhere.[1,2] Briefly, DCS measures fluctuations of light emerging from the tissue and computes it temporal autocorrelation. It then uses the characteristic decay time of the temporal autocorrelation function in order to provide a blood flow index (BFI) which is related to the motion of the red blood cells.[2,3] BFI is extracted as an expression of α times the Brownian motion diffusion coefficient D_b in cm^2/s. Here, α describes the fraction of photon scattering events solely from the moving scatterers such as red blood cells in the tissue. In this manuscript, CBF is expressed as a percentage of αD_b relative to its mean.

For this study a custom built in-house DCS device was used. It used a single long-coherence length laser at 850 nm wavelength and a sampling rate of 50 Hz, high enough to retrieve cardiac pulsation. The optical probe used for this study allowed for the integration of DCS as well as Near Infrared Spectroscopy (NIRS). Like DCS, NIRS is another form of diffuse optical technique utilizing near infrared light, however, NIRS is sensitive to changes in hemoglobin concentrations in blood instead of its flow rate like the DCS. Data collected from NIRS were not used in this manuscript. The probe was designed and fabricated by Fiberoptic Systems Inc. (CA, USA). Skin irritation was avoided by the use of 1/16" thick cushioning foam (#8722K97, McMaster-Carr, Aurora, OH, USA). A black cloth was used to cover the probe and the region surrounding it during measurements to obstruct the room light. Care was taken such that the cloth remained in place or adjusted following any movement of the patient. The DCS source-detector distance was 20 mm.

Section 2. Signal processing

In obtaining SNR, fast Fourier transform (FFT) of the CBF time series was used to determine heart rate and its harmonics, and noise. The signal was defined as the mean of DCS signal strengths at the heart rate and up to the second harmonics, and the noise was defined as the DCS signal strength 1 Hz beyond the second harmonics at which no signs of cardiac pulsation was observed. Based on empirical evaluation, only DCS sessions with SNR $\geq$ 4.8 were included in this manuscript.

For each DCS measurement session, first z-score rejection was used to eliminate any large or unwanted artifacts in CBF time series. This z-score value varied from patient to patient depending on the type of artifacts. The CBF time series was then filtered with a high pass Butterworth filter of 7th-order at 0.5 Hz to remove respiration signal. At this step, the signals obtained from the patient monitor [invasive ICP (ICP_{inv}) : 120 Hz, electrocardiogram (EKG) : 240 Hz, and mean arterial pressure (MAP) : every 30 min] were resampled to 50 Hz to match the sampling frequency of CBF.

At the onset of a measurement session, a time marker was sent to the DCS system through the auxiliary port. Simultaneously, the time at the bedside monitor was manually noted, which was later used to synchronize all signals in time by aligning with the time marker. Further alignment was achieved by cross-correlating the cardiac pulsation recorded in CBF and EKG. CBF was additionally filtered with a moving average filter of 0.1 seconds to further remove noise.

In the next step of data processing, individual CBF pulses were segmented out each from its time series. Since CBF can be subject to instrument noise and movement, the strong R-peaks in EKG were used to determine start and end of a pulse. At this step, to eliminate outliers, the algorithm was programed to calculate z-score across all pulses in time for the duration of a pulse, and pulses with z-score > 3 were rejected. On an average across all patients, 12% of the individual CBF pulses were considered outliers and omitted by the z-score rejection. To further improve SNR, using a moving average filter, 100 pulses (150 pulses for patients with average SNR < 7) were averaged to generate an average CBF pulse. The process was repeated after a shift of 10 pulses (15 pulses for patients with average SNR < 7), and thus a series of average CBF pulses were obtained from the CBF time trace. It is to note that, the averaging of the CBF pulses with the shift of 10 - 15 pulses make it difficult to delineate what percentage of the acquired DCS data in

time was filtered out as outliers by the z score filtration and what percentage was finally used for ICP prediction. In that regard, the 'hours analyzed' information in the last column of Table 1 and the average heart rate of the patient obtained with EKG were analyzed to obtain how many average CBF pulses could have been extracted without the z-score filtration. This information explains how much of the acquired DCS data had to be sacrificed to obtain good signal quality. We observed, on an average across all patients, 21% of the total average CBF pulses implemented in the model for ICP prediction (#19,019) were rejected by z-score filtration.

To account for different heart rates across patients, the CBF pulse averages were normalized in time (x-direction). To do that, the width of the pulse average was set to be 151 data points (chosen arbitrarily) between 0 to 1 from one diastolic point to the next in time. To improve the SNR further in CBF, an adaptive Kalman filter was applied. The pulse averages were then normalized in amplitude (y-direction) such that pulses started at zero amplitude at the onset (diastole) and reached a maximum height of 1 at the systolic point. This made the CBF pulse averages comparable in amplitude across patients.

Following that, morphological features were extracted from each processed CBF pulse average using the 'findpeaks' function in Matlab (MathWorks, USA). Any pulse amplitude less than zero, observed occasionally towards the pulse tail, were not included in obtaining area under the curve feature of the pulse. Details of the pulse morphology are described in our previous work.[1] Briefly, P_1, P_2 and P_3 refer to the percussion, tidal and dicrotic peaks respectively. In cases when a feature was not detectable, e.g. merging of P_1 and P_2 at high ICP leading to no detectable P_3,[4] the undetected features were set to 0. These features were still used in the machine learning algorithm as the lack of a peak could be a strong indicator of elevated ICP.

Section 3. Regression learner

In this step, a train/test split ratio of 80/20 was used. Due to random splitting, train and test sets maintained a similar distribution of ICP_{inv}. The random decision forest was built using the python toolbox scikit-learn.[5] The working principle of regression forests and random decision forests in general has been described previously.[6,7] In this work, 200 individual decision tree regressors were used to build the random forest model. This number was chosen empirically, after an analysis between 1 and 400 trees showed that the algorithm performance reached an asymptote by around 100 trees and slowly improved from there. To further limit overfitting, the maximum depth of each tree was set to 20. Due to the overall large sample size, no cross validation was performed.[8] The total computation time for training and testing (#19,019 samples with train/test split ratio of 80/20) was found to be 1.06 seconds on a computer with AMD Ryzen 7 3800X 8-Core 3.89 GHz processor and 32.0 GB RAM.

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